# Encephalopathy Due to Severe Hyponatremia in an Ultramarathon Runner

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ACUTE HYPONATREMIA has been noted in some athletes after they participated in endurance exercise. Although the ingestion of hypotonic fluid combined with sodium chloride losses in sweat has been most commonly implicated as the cause of this syndrome, its pathogenesis is unclear because of fragmentary laboratory data. We present a case of severe hyponatremia with life-threatening encephalopathy that developed in an ultramarathon runner after he dropped out of a race because of foot blisters. The patient showed clear evidence of volume expansion and had a documented abnormality in urinary dilution. We postulate that much of the ingested water was absorbed only after he discontinued exertion and was retained because of the continued secretion of antidiuretic hormone (ADH). The ingestion of a nonsteroidal anti-inflammatory drug before the marathon may have exacerbated the urinary defect in dilution.

## Report of a Case

The patient, a 57-year-old man, came to medical attention after a seizure occurred one hour after he completed 88.5 km (55 mi) of a 161-km (100-mi) ultramarathon. The patient had previously been in excellent health. He had taken ibuprofen for several days to relieve mild arthralgias, but was taking no other medication. His weight at the start of the race was 72 kg. During the race he drank 12 liters of a glucose and water solution. After running 64 km (40 mi), his weight was 74 kg. He dropped out at 88.5 km because of severe blisters on both feet. Approximately 45 minutes later, he became confused and disoriented, his speech became slurred, and he had a generalized seizure. In the emergency department his temperature was 36°C (96.8°F), his pulse was 69 beats per minute, blood pressure 146/86 mm of mercury, and respirations 14 per minute. He had decorticate posturing. His optic discs were flat, pupils were equal and reactive to light, and corneal reflexes were present. Deep tendon reflexes were brisk and symmetric, and Babinski's sign was present on both sides. The patient withdrew to deep pain but did not localize to voice or follow commands. His neck veins were distended to the angle of the jaw. There were no clinical signs of dehydration. Blisters were present on both feet. The physical examination otherwise showed no abnormalities.

**ABBREVIATIONS USED IN TEXT**
ADH = antidiuretic hormone
ECF = extracellular fluid volume

Initial laboratory tests elicited the following values: hematocrit, 0.38; serum electrolytes: sodium, 119, potassium, 3.6, and chloride, 89 mmol per liter; total carbon dioxide, 13 mmol per liter (13 mEq per liter); urea nitrogen, 5 mmol per liter (14 mg per dl); creatinine, 100 μmol per liter (1.1 mg per dl); glucose, 8.1 mmol per liter (146 mg per dl); osmolality, 248 mmol per kg of water. Urine osmolality was 474 mmol per kg of water and urine sodium, 39 mmol per liter. Arterial blood gas results with the patient breathing 2 liters of oxygen by nasal cannula were pH 7.43, $P_{CO_2}$ 4.5 kPa (34 mm of mercury), and $P_{O_2}$ 16.0 kPa (120 mm of mercury). The electrocardiogram showed sinus rhythm with a rate of 75 per minute; nonspecific ST and T-wave abnormalities were present. A chest x-ray film and a noncontrast computed tomographic scan of the head were normal. After the patient returned from the computed tomographic scan, anisocoria was noted, with the right pupil 6 mm and the left pupil 2 mm; both pupils reacted sluggishly to light. The serum sodium was again measured and was 111 mmol per liter.

Furosemide, mannitol, and a 3% solution of saline were administered intravenously. Twelve hours after admission the patient remained obtunded, although the anisocoria had resolved. The serum sodium level was 125 mmol per liter. On the second hospital day, the patient was somnolent but would localize to voice. Over the next four days, he gradually recovered and was discharged.

## Discussion

Hyponatremia is an underrecognized complication of endurance exercise. Hiller and co-workers reported that 19 of 64 (30%) finishers in the 1984 Hawaiian Ironman triathlon had an abnormally low postrace serum sodium concentration.[1] Noakes and associates described the development of hyponatremic encephalopathy in four athletes during endurance events lasting longer than seven hours.[2] Urine osmolality was increased in the one patient for whom this value was reported. More recently, Frizzell and colleagues described the development of hyponatremic encephalopathy in two runners competing in the 1983 American Medical Joggers Association ultramarathon race.[3] No values for urine sodium or osmolality were reported for either patient.

Our patient presented with acute hyponatremic encephalopathy and had clinical and laboratory findings consistent with water intoxication.[4] The severe hyponatremia was not associated with clinical evidence of volume depletion. The patient had gained 2 kg in weight and did not have tachycardia or hypotension. In fact, his vascular volume seemed to be increased based on the finding of neck vein distention. In addition, he was excreting sodium in his urine despite severe hyponatremia. The

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urine osmolality and sodium concentration were consistent with ADH effects despite his apparent volume-expanded state.

An intriguing aspect of this disorder is the time course of symptoms and hyponatremia. The patient was asymptomatic until almost an hour after he stopped running, and his serum sodium level fell from 119 to 111 mmol per liter during the first hour of hospital admission without his receiving any hypotonic fluids. Splanchnic ischemia, which may impair enteral absorption, can occur during endurance exercise.[5] It is possible, therefore, that part of the water ingested by our patient was not absorbed while he was running. With the cessation of exercise and reperfusion of the splanchnic bed, this sequestered water could have been absorbed rapidly, worsening his hyponatremia and expanding his body fluid volume. Although this seems a likely explanation for the abrupt fall in his serum sodium level, continued ADH secretion is required for the absorbed water to be retained.

Hyponatremia after endurance exercise has been attributed to sodium and water losses in sweat and replacement with water.[2,5] According to this view, urinary water retention results from ADH secretion stimulated by a reduction in extracellular fluid (ECF) volume occurring as a consequence of sodium loss. If this construction is correct, the urine sodium concentration should be vanishingly low. In this patient, however, the urine sodium level of 38 mmol per liter was consistent with the evidence on physical examination of a normal or increased ECF volume. It is possible that the physical stress of endurance exercise results in continued ADH secretion after the cessation of exercise, even when the ECF volume is expanded and hyponatremia is present. Various stresses including pain, hypoxia, hypercapnia, and hypoglycemia have been associated with ADH secretion and hyponatremia.[4] Clearly more work needs to be done to characterize the factors responsible for this syndrome. Our patient had been taking ibuprofen, a prostaglandin inhibitor. Severe hyponatremia has been reported with the use of this class of drugs,[6,7] presumably because prostaglandin is a normal antagonist to the hydroosmotic effect of ADH. Whether this drug was a contributing factor in the development of hyponatremia in our patient is unknown.

The treatment of hyponatremia with an isotonic or hypertonic saline solution is critically important when notable encephalopathy is present.[4,8,9] If there is evidence of ECF volume expansion, furosemide is a useful therapeutic adjunct through its effect of reducing the ECF volume and allowing the subsequent retention of administered sodium.[10] Its use can be hazardous, however, if the ECF volume is reduced. An improved understanding of the role of sodium chloride loss, fluid replacement, and ADH secretion in this life-threatening complication of ultramarathon competition is needed to develop a rational approach to treatment and, more important, to prevent its development. Given the findings in one patient, we recommend that athletes be cautioned regarding the overzealous ingestion of water during endurance exercise. They should also be cautioned about the possible effects of nonsteroidal anti-inflammatory drugs on renal function and urinary dilution.

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# Use of Aprotinin to Reduce Intraoperative Bleeding

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BLEEDING DURING a surgical procedure is a common problem associated with both morbidity and death of surgical patients in the United States; it increases the risk of multisystem organ failure and death. Transfusion therapy is associated with the additional risks of allergic reaction and the transmission of infectious diseases such as hepatitis and the acquired immunodeficiency syndrome. Despite tremendous advances in blood banking, public concern about the safety of America's blood supply has substantially increased the fear of transfusion for many patients having surgical treatment.

The use of aprotinin, a serine protease inhibitor, has been shown recently to reduce dramatically the blood loss in operations that involve cardiopulmonary bypass and in other cardiac operations.[1-7] Several of the studies showing efficacy and safety have been randomized, placebo-controlled trials.[1-4,6] The drug is now used extensively in Europe and the Middle East for cardiac surgery. Although the mechanism of action has not been clearly established, it appears that aprotinin improves platelet function, which is impaired following cardiopulmonary bypass.[7,8] Apro-

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